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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,943	03/08/2000	KUBER T. SAMPATH	CIBT-P01-570	7342

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EXAMINER	
ANDRES, JANET L	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,943	SAMPATH ET AL.	
	Examiner	Art Unit	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-29 and 76* is/are pending in the application.

4a) Of the above claim(s) *5,29 and 76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6 and 8-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO AMENDMENT

1. Applicant's amendment filed 26 September 2003 is acknowledged. Claims 1, 3, 5-29, and 76 are pending in this application. Claims 5, 7, 29, and 76 are withdrawn from consideration as being drawn to non-elected inventions; claim 7, which does not encompass the elected species of renal tissue, was inadvertently omitted from the listing of withdrawn claims in the previous office action but was not examined. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

2. The objection to the specification is withdrawn in response to Applicant's amendment.

3. The rejection of claims 1, 3, 6, 8-22 and 28 under 35 U.S.C. 112, first paragraph, as containing new matter in the form of the phrase "non-neuronal" is withdrawn in response to Applicant's amendment.

4. The rejection of claims 1, 3, and 8-28 under 35 U.S.C. 112, first paragraph, as lacking enablement for morphogens is withdrawn in response to Applicant's argument that the specification describes a subfamily of the TGF-β superfamily and because morphogens are generally recognized in the art as being members of the BMP subfamily.

5. The rejection of claims 1, 6, 12-15, and 23-28 under 35 U.S.C. 102(b) as being anticipated by WO 93/04692 is withdrawn in response to Applicant's argument that WO 93/04692 does not teach comparison to a positive control.

6. The rejection of claims 8-11, 21, and 22 under 35 U.S.C. 103(a) as unpatentable over WO 93/04692 is withdrawn for the reasons set forth in paragraph 5 above. These claims depend from 1 and thus the same argument is relevant. It is noted that this rejection was also intended to

apply to claim 3, which is discussed in paragraph 12 of the previous office action but was inadvertently omitted from the first sentence, as well as claims 16-19, whose limitations were discussed but which were not included in the rejection.

Claim Rejections Maintained/New Grounds of Rejection

7. The rejection of claims 1, 3, 6, and 8-28 under 35 U.S.C. 112, second paragraph, as indefinite in the recitation of "analog" or "variant" is maintained for reasons of record in the office action of 16 June 2003.

Applicant argues that "analog" is defined and points to several pages in the specification. Applicant additional argues that "variant" is defined and points to several pages in the specification. Applicant argues that no undue experimentation is required.

Applicant's arguments have been fully considered but have not been found to be persuasive. There is no definition of "analog". What is provided are "general terms", "functional equivalent" with no definition of function, language including agents that are not related to the morphogens, and many other molecules having many different functions. The cited paragraphs do not provide a description of what an analog is and what it is not. There is no limiting definition; nothing is excluded and anything may be included. Thus one of skill in the art would not be able to determine the metes and bounds of these claims. This is a rejection under of the claims under 35 U.S.C. 112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, not a rejection as lacking enablement. "Undue experimentation" is not a factor in the question of whether the artisan would be able to determine what Applicant intended to claim. By reading the claims and the specification, the skilled artisan would not be able to determine what

molecules Applicant intended to include and what molecules Applicant intended to exclude. Similarly, "variant" is not defined. The paragraph cited by applicant includes the phrase "without limitation". Thus, clearly, one of skill in the art would not be able to determine the metes and bounds of the claimed invention.

8. Claims 1, 6, 12-15, 20, and 23-28 are newly rejected under 35 U.S.C. 103(a) as unpatentable over WO 93/04692 in view of U.S. patent 6,096,706 (Toback et al, filed 1997).

As was stated in the office action of 16 June 2003, WO 93/04692 teaches models for evaluating morphogens *in vivo* in surgically-induced renal ischemia-reperfusion injury, followed by parental administration of the morphogen, on p. 77, anticipating the limitations of claims 1, 6, 12, 15, 20, and 23-28. That these morphogens include those claimed by Applicant is set forth in table II, pages 44-49. Variants are taught on pp. 34-35. Intravenous administration is taught in a cardiac model on pp. 70 and 73, anticipating claim 13. Oral administration is taught on p. 81, anticipating claim 14. WO 93/04692 also teaches other means of administration on p. 51. WO 93/04692 fails to teach use of controls, as provided in step D. The '706 patent teaches the use of a renal failure assay to compare different peptides in order to evaluate which is most effective. See example 1, column 26, lines 41-56. The most effective was subject to further *in vivo* study; see column 6, lines 56-66, and column 27 and 28, as well as example 5, lines 26-64. It would have been obvious to one of ordinary skill in the art to combine the teachings of WO 93/04692 with those of the '706 patent to modify the assays of WO 93/04692 to include comparison to a positive control. One of ordinary skill would have been motivated to do so because the '706 patent uses a similar approach to decide which of several compounds is most potent, and one of ordinary skill would readily appreciate that a similar modification could be made to the assays

used by WO 93/04692, to compare morphogens to one which was known to function for the purposes of identifying those worthy of further, more extensive *in vivo* study, as taught by the '706 patent.

Most of Applicant's arguments with respect to the rejection under 35 U.S.C. 102(b) are not relevant to the new rejection under 103(a). However, Applicant argues that WO 93/04692 does not teach variants or analogs (p. 12, lines 1-2). This is not found persuasive because WO 93/04692 does in fact teach proteins of limited homology on p. 34-35.

9. Claims 3, 6, and 8-28 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/04692 in view of U.S. patent 6,096,706 and further in view of Benet et al.

WO 93/04692 and U.S. patent 6,096,706 teach as set forth above but fail to teach dosage optimization, as claimed in claim 3 and claims 6 and 8-28 by dependency, different times, as claimed in claims 16-19, or evaluation in compromised animals, as claimed in instant claims 8-11, 21 and 22. However, it would have been obvious to one of ordinary skill to evaluate treatment parameters such as time of administration and administration to compromised animals. Optimization of treatment protocols is art standard: Benet and Sheiner teach conditions including age and disease as affecting drug administration. Further, WO 93/04692 teaches evaluation of administration "at various times prior to or following occlusion and/reperfusion". Evaluation of morphogens in fibrosis is taught in an *in vitro* model on pp. 83-86. The need for dosage optimization is addressed on p. 59. WO 93/04692 thus teaches a model for evaluating the effects of morphogens on renal damage, and further teaches several factors important for therapeutic administration. Thus it would have been obvious to one of ordinary skill to evaluate morphogens using the method of WO 93/04692 as modified by the '706 patent at different times, in different

doses, and in different disease states; one of ordinary skill would have been motivated to do so because WO 93/04692 explicitly suggests different time points, doses, and means of administration, and because altered effects in disease states are well known in the art, as taught by Benet and Sheiner. Thus one of ordinary skill would have readily perceived that these parameters should be evaluated in order to optimize administration and completely evaluate therapeutic utility.

Applicant argues with respect to the previous rejection of these claims that the claims require comparison to a positive control; this argument is not relevant to the current rejection, as stated in paragraph 8 above. Applicant further argues that the instant specification teaches that it would be easier to evaluate morphogen activity in older animals, but that WO 93/04692 is completely silent about older animals and that the cited art would not suggest a predisposition as to which would be better. Applicant concludes that the prior art thus fails to suggest all of the claimed limitations and that there would be no reasonable expectation of success. Applicant additionally argues that different disease conditions would have different effects on morphogen activity and thus there would be no reasonable expectation of success.

Applicant's arguments have been fully considered but have not been found to be persuasive. The motivation to combine references need not be Applicant's. As is stated above, WO 93/04692 teaches a therapeutic utility and Benet and Sheiner teach that various conditions affect therapeutic results. Thus one of ordinary skill in the art would be motivated to combine the references for precisely the reason set forth in Applicant's arguments. One of ordinary skill would not be able to predict what the effects of the various conditions would be on therapeutic

utility and would thus have to test them to ascertain whether the morphogens would work in animals afflicted with such conditions.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
December 17, 2003